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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/779,304	02/13/2004	Sheng-He Huang	CIP2411A-SHH	7978

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RAYMOND Y. CHAN
108 N. YNEZ AVE., SUITE 128
MONTEREY PARK, CA 91754

EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/779,304	HUANG, SHENG-HE	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *3-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☒ Claim(s) *1 and 2* is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2 and 3-17 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-2 in the reply filed on February 22, 2006 is acknowledged.

2. Claims 3-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups II and III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 22, 2006.

Sequence Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this office action. A complete response to this office action should include compliance with the sequence rules. Failure to fully comply with this requirement in the time period set forth in this office action will be held non-responsive.

4. Figures 1, 10, 11 and 12, as well as Tables 2 and 3 need SEQ ID Nos assigned and inserted to each of the sequences that fall within the sequence compliance rules.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-2 of this application conflict with claims 1-2 of Application No. 10/123,965. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claim Objections

2. Claims 1 and 2 are objected to because of the following informalities:

3. Claim 1 recites abbreviations: "BMEC" and "ibeA", that should be defined in the claims upon their first appearance in the claims.

4. Claim 2, paragraph (f) recites "combining a ibeA" ; "a" should be ----an---.

5. Claim 2, paragraph (f) also recites the phrase "to a ibeA"; "a" should be -----an----.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 functionally define the term "identifying" for representing reagents which functionally define "structures (paragraphs (a), (b))" and " combining ..... to a ibeA" to provde a complete nucleic acid sequence for a gene. Additionally, it is not clear how the conducting step of analysis is being carried out because what is being used in the test is not positively recited in step (g). While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al (November 1995) in light of evidenced provided by Huang et al (1999).

10. Huang et al disclose the instantly claimed invention directed to a method of providing a complete nucleic acid sequence which encodes a ibeA gene, the method comprising the steps of:

a. **identifying** Escherichia coli structures that contribute to the invasion of BMEC to a ibeA (see page 4470, col. 1, paragraph 3 "To facilitate the identification of the genes contributing to E.coli invasion of BMEC, we used transposon TnphoA to generate a collection of noninvasive E.coli mutants.");

b. **extracting and purifying** said ibeA from said Escherichia coli structures (see page 4471, col. 2, "DNA sequencing and analysis", paragraph 4; which provided means for the recombinant expression of ibeA protein (Huang et al 1999 states ibeA is also known as ibe10, col. 2, paragraph 2, middle of paragraph) which allowed the expression, extraction and purification of ibeA protein (see page 4471, col. 1, paragraphs 2-3).

c. **Analyzing** said extracted and purified ibeA (see page 4471, col. 2 paragraph 4 "Both strands of the DNA were sequenced to ensure accuracy, and the sequence data were analyzed with the DNA analysis protein developed by the Genetics Computer Group" and the extracted and purified protein ibeA was analyzed by SDS-PAGE, Bio-Rad protein assay, and "effect on invasion of BMEC by strain RS218, page 4472, col. 1, paragraph 3);

d. **Determining** the complete nucleic sequence of ibeA (see page 4472, col. 2, paragraph 2, GenBank accession number L42624).

Huang et al (1995) inherently anticipates the instantly claimed invention in light of evidence provided by Huang et al that shows the nucleic acid of Huang et al (1995) to encode a gene that contributes to invasion.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al (1995) as applied to claim 1 above, in view of Huang et al (1999).

See discussion of Huang et al (1995) above. Huang et al teach, show and carry out a method of providing a complete nucleic acid sequence encoding ibeA gene (also known as ibe10), by:

e. generating mutant strains of E.coli that comprise genetic mutations in the ibeA open reading frame (see page 4470, col. 2, last paragraph "mutagenesis of E.coli K1 RS218"),

f. combining ibeA mutant strains (M15, is an E.coli strain that lacks an active ibeA gene, see Table 1, laboratory strain of Qiagen) with ibeA to form transformants (see page 4472, col. 1, paragraph 2 "Expression constructs"; Electrocompetent E.coli strains were made by transformation with the coding sequence for IbeA (also known as Ibe10) and

g. conducting complementation analysis to test an invading ability to BMEC (the expressed IbeA from the transformed strain was used to evaluate invasion of BMEC with a IbeA positive strain (see RS218 assay with IbeA, page 4472, col. 1, paragraph 3).

Huang et al (1995) teaches mutants of the ibeA gene open reading frame; complementation of a strain of E.coli with the coding sequence for ibeA; and analysis testing of invading ability to BMEC utilizing wild type strains, and mutant strains, as well as wild type strains in the presence of expressed IbeA from complemented transformed strains of E.coli but differs from the instantly claimed invention by failing to show the mutant strain to be an in-frame deletion mutant; and the utilization of the complemented strain in the analysis assay for invading ability.

Huang et al (1999) teach the production of in-frame deletion mutant (see page 2107, col. 1, paragraph 2) strains of E.coli for ibe genes and the complementation (see page 2107, col. 1, paragraph 5) of the deletion mutant with the complementary coding sequence in an analogous art for the purpose of showing the restoration of invasion ability of BMEC of the ibe deletion mutant and introduction of invasive ability into non-invasive strains of E.coli.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the ibe mutant of Huang et al (1995) that was an insertion mutant, to be an ibe deletion mutant as taught by Huang et al (1999) for analysis testing of invading ability to BMEC because both Huang et al (1995 and 1999) are directed to the identification of genes and gene products of invasive E.coli strains through generating mutant strains that have lost their invading ability and carry out analysis testing for invading ability using expressed ibe gene products, and Huang et al (1999) positively showed the restoration of invading ability to BMEC through complementation of the ibe deletion mutant strain and to show that the ibe gene and its product was "truly responsible for the" invasive phenotype and the noninvasive phenotype was truly induced through the deletion of the ibe gene.

In the absence of a showing of unexpected results, Huang et al (1995) in view of Huang et al (1999) obviate the instantly claimed invention directed to a method of that provides a complete nucleic acid sequence for a gene of an ibeA gene cluster because Huang et al (1995) discloses the importance of identifying E.coli structures that contribute to invasion of BMEC and Huang et al (1999) teaches, shows and provides motivation for the production of deletion mutants in order to positively determine how an ibe gene product truly effects the invasive

phenotype through in-frame deletion and complementation, coupled with analysis testing of BMEC invading ability.

Huang et al (1995) in view of Huang et al (1999) obviate the instantly claimed invention.

Conclusion

1. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

2. Badger et al (April and September 2000) are cited to show methods of identifying genes contributing to invasion across the blood brain barrier.

3. Huang et al (August 2000, section 4.1, Microbes and Infection) is cited to show the generation of deletion mutant strains of ibe genes and their complementation to restore invading ability.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
May 16, 2006

L. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600